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ABSTRACT

Data collection has been completed and data analysis is in progress for all of the human studies outlined in this proposal. Findings to date include 1) lack of changes in attention and memory functions during pregnancy and lactation, 2) lack of difference in hormonal and anxiety responses to psychological stress, 3) enhanced lymphocyte proliferation and insensitivity to cytokine suppression by glucocorticoids in lactating women, and 4) increased blood pressure in postpartum, nonlactating women.

Data collection is in progess for animal studies outlined in this proposal. Consistent with the human studies described above, enhanced lymphocyte proliferation has been found in lactating rats compared to nonlactating rats and virgins.

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Sue Carter 9-30-96

PI - Signature Date

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INTRODUCTION

The purpose of this research project "Lactation and Reactivity to Physical and Psychological Stress" is to determine the effects of lactation on several different components of stress responses in both humans and animal models. Specific studies are in progress in humans to assess the effects of lactation on cognition, immune responses to inflammatory antigens, and hormonal, physiological and anxiety responses to psychological stress. In rats, parallel studies are in progress to measure immune responsivity, and behavioral, hormonal and physiological responses to physical and psychological stressors. In addition studies are planned in rats to attempt to identify the specific lactational hormones which generate the apparent reductions in behavioral and physiological responses and increased inflammatory responsivity during lactation.

BODY

Aim 1. Human Research: Cognitive performance

Recruitment, screening and cognitive testing of 20 control subjects, 20 pregnant subjects, 20 postpartum lactating subjects and 20 postpartum nonlactating subjects has been completed using both the selective attention and the implicit/explicit memory paradigms outlined in the original proposal. Data analysis has been completed for the selective attention test, and showed no difference between any of the 4 subject groups. Because of this, we do not plan to retest the lactating women after weaning. Analysis of the implicit/explicit memory data is in progress. If differences in memory testing are found in the lactating women, they will be retested after weaning. We expect to complete these analyses, and additional testing if indicated, and to submit both studies for publication in the coming year.

Aim 2. Human Research: Endocrine and immune effects of psychological stress

Recruitment, screening and testing of 15 control subjects, 23 lactating and 15 postpartum nonlactating women has been completed. Psychological stress testing was performed as described in the original proposal using the Trier Social Stress Test. In response to the stress interview, all three groups of subjects showed

significant increases in anxiety, heart rate, systolic and diastolic blood pressure, and ACTH and cortisol secretion. Data analysis completed to date shows no difference in the hormonal (ACTH and cortisol), heart rate or anxiety responses to psychological stress among the three conditions. However, blood pressure at baseline and during stress was significantly elevated in the postpartum, nonlactating women.

Several changes in immune function were noted in post-partum women. Compared to control women, both lactating and nonlactating post-partum women had increased lymphocyte proliferation to a T-cell mitogen (PHA) at baseline and throughout the psychological stress test. Post-partum women did not show the usual decrease in proliferation during stress. Similarly, postpartum women did not show the normal decrease in proliferation in response to a B-cell mitogen during stress. Baseline response to the B-cell mitogen (pokeweed) was reduced in both groups of post-partum women. In addition, post-partum, nonlactating women had elevated total white blood cell counts with a normal distribution of white cell subpopulations. Finally, in a separate *ex vivo* study, lipopolysaccharide stimulated cytokine (IL-1 and IL-6) release was resistant to dexamethasone suppression in lactating women compared to controls. Cytokine assays and data analysis of samples from bottle-feeding women and pregnant women is in progress. We expect to submit these studies for publication in the coming year.

Aim 3. Animal Research: The behavioral effects of lactation

We have refined the testing paradigm for conditioned freezing in our laboratory and found a reduction in conditioned freezing behavior and in the ACTH and corticosterone responses to conditioned freezing in lactating rats. We also have established the plus maze testing paradigm in our laboratory and found increased exploration of the open arms of the maze in lactating rats.

Aim 4. Animal Research: Possible mechanisms for the behavioral and physiological effects of lactation

Our technician is currently being trained to insert intracerebroventricular cannulas and to perform radioimmunoassays to enable data collection for these studies. Two behavioral paradigms to be used in these studies have been established in our laboratory as described above, and reliability testing with two

additional paradigms, swim stress and open field, is in progress. We did not find a difference in acoustic startle reactions in lactating vs. nonlactating rats, so acoustic startle will not be used for dissection of the hormonal mechanisms underlying reduced stress responses and reduced fear behaviors in lactating rats. Instead we will use the conditioned freezing paradigm to model psychological stress or fear.

CONCLUSIONS

1. Cognition, as measured by selective attention and implicit and explicit memory tasks is not affected by pregnancy or lactation.

2. Lactation does not affect the anxiety, endocrine, heart rate or blood pressure responses to psychological stress.

3. Compared to control women, lactating women are resistant to glucocorticoid suppression of pro-inflammatory cytokines.

4. Compared to control women, both lactating and nonlactating postpartum women are resistant to stress-induced suppression of lymphocyte proliferation.

5. Lactating rats show less fear behavior and less stress hormone responsivity in animal models of anxiety. Lactating rats do show reduced conditioned freezing responses and increased exploration in a novel environment. Lactation does not affect acoustic startle responses in rats.

6. Lactating rats have enhanced lymphocyte proliferation in response to T-cell mitogens.

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Redwine L, Altemus M, Sternberg E, Gold PW, Carter CS. Lactation increases lymphocyte proliferation responses in rats. Poster to be presented at International Society for Neuroimmunomodulation, Bethesda, MD, November, 1996.

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